any significant chemical, physical, or other change or deterioration of the drug; or any failure of one or more distributed batches to meet specifications established in the new animal drug application or in the antibiotic regulations, this information shall be submitted. Any unresolved experience of the kinds listed in this paragraph shall be reported even though it occurred before the 2-year period.

(2) If the new animal drug is no longer marketed, but it is the subject of an approval that is still in effect:

(i) Identification of the dosage form of the new animal drug or medicated feed premix by its established and proprietary names, if any;

(ii) The formula showing quantitatively each ingredient of the drug to the extent disclosed on the label (a copy of the label will ordinarily fulfill this requirement);

(iii) The route of administration;

(iv) The new animal drug or other identification or application number;

(v) The date and reason for discontinuing its marketing.

(c) Approval of applications covering products which are no longer marketed may be withdrawn under §514.115 of this chapter on the basis of a request for its withdrawal submitted in writing by a person holding an approved application. Such withdrawal of approval will be made on the ground that the drug subject to such application is no longer being marketed, provided information is furnished in support of this finding and provided certain other conditions exist as specified in that section. A written request for such withdrawal will be construed as a waiver of an opportunity for a hearing.

(d) Sponsors of new animal drugs identified in paragraph (a) of this section are exempt from the reporting requirements of this section if:

(1) Their product is no longer marketed, and information has previously been submitted to the Food and Drug Administration regarding discontinuation of marketing including the date and reason for such action, and any existing approval for the product has been withdrawn; or

(2) As a result of a supplemental approval granted beginning June 20, 1963, the sponsor is presently reporting under the requirements of §510.300.

(e) After the submission of the initial reports required by paragraph (b) of this section, each sponsor shall maintain records and submit yearly reports of the kinds required by §510.300.

(f) All reports required by this section shall be addressed to the Division of Surveillance (HFV–210), Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, and shall be distinctly marked ''New Animal Drug (or Antibiotic) Report'' together with the applicable new animal drug application number, antibiotic account number, or other identification on the envelope.

[45 FR 42261, June 24, 1980, as amended at 54 FR 18280, Apr. 28, 1989; 57 FR 6475, Feb. 25, 1992]

Subpart E—Requirements for Specific New Animal Drugs

§510.410 Corticosteroids for oral, injectable, and ophthalmic use in animals; warnings and labeling requirements.

(a) The Food and Drug Administration has received reports of side effects associated with the oral, injectable, and ophthalmic use of corticosteroid animal drugs. The use of these drugs administered orally or by injection has resulted in premature parturition when administered during the last trimester of pregnancy. Premature parturition may be followed by dystocia, fetal death, retained placenta, and metritis. Additionally, corticosteroids used in dogs, rabbits, and rodents during pregnancy have produced cleft palate in offspring. Use in dogs has resulted in other congenital anomalies, including deformed forelegs, phocomelia, and anasarca. Drugs subject to this section are required to carry the veterinary prescription legend and are subject to the labeling requirements of §201.105 of this chapter.

(b) In view of these potentially serious side effects, the Food and Drug Administration has concluded that the labeling on or within packaged corticosteroid-containing preparations intended for animal use shall bear conspicuously the following warning statement:

Warning: Clinical and experimental data have demonstrated that corticosteroids administered orally or by injection to animals may induce the first stage of parturition if used during the last trimester of pregnancy and may precipitate premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

Additionally, corticosteroids administered to dogs, rabbits, and rodents during pregnancy have resulted in cleft palate in offspring. Corticosteroids administered to dogs during pregnancy have also resulted in other congenital anomalies, including deformed forelegs, phocomelia, and anasarca.

[49 FR 48535, Dec. 13, 1984]

§ 510.413 Chloroform used as an ingredient (active or inactive) in animal drug products.

(a) Chloroform has been used as an ingredient in animal drug products such as cough preparations, linaments, and some pastes. Although considered safe for many years, recent information has become available associating chloroform with carcinogenic effects in animals. Studies conducted by the National Cancer Institute have demonstrated that the oral administration of chloroform to mice and rats induced hepatocellular carcinomas (liver cancer) in mice and renal tumors in male rats.

(b) Any drug product intended for use in or on animals and containing chloroform as an ingredient is deemed to be either (1) a new animal drug within the meaning of section 201(v) of the act, and unsafe within the meaning of section 512 of the act and adulterated under section 501 of the act and subject to regulatory action under sections 301, 501, and 512 of the act; or (2) misbranded under section 502 of the act, and therefore subject to regulatory action under sections 301 and 502 of the act. Any animal drug product containing chloroform in residual amounts from its use as a processing solvent during manufacture of the drug product, or from the synthesis of a drug ingredient, is not, for the purpose of this regulation, considered to contain chloroform as an ingredient.

(c) Any holder of an approved new animal drug application for a drug product containing chloroform as an ingredient shall submit to the Food and Drug Administration on or before October 3, 1977, a supplemental application providing for a revised formulation removing chloroform as an ingredient.

(1) The supplemental application shall contain:

(i) A full list of articles used as components and a full statement of the composition of the drug product.

(ii) The date that the composition of the drug product will be changed.

(iii) Data showing that the change in composition does not interfere with any assay or other control procedures used in manufacturing the drug product, or that the assay and other control procedures are revised to make them adequate.

(iv) Data available to establish the stability of the revised formulation and, if the data are too limited to support a conclusion that the drug will retain its declared potency for a reasonable marketing period, a commitment from the applicant:

(*a*) To test the stability of marketed batches at reasonable intervals;

(*b*) To submit the data as they become available; and

(*c*) To recall from the market any batch found to fall outside the approved specifications for the drug.

(v) Copies of the label and all other labeling to be used for the drug product—a total of nine copies if in final printed form, three copies if in draft form.

(2) If such drug product contains more than 1 percent chloroform, the revised formulation containing no chloroform shall not be marketed before the receipt of written notice of approval of the supplemental application by the Food and Drug Administration.

(3) If such drug product now contains 1 percent or less chloroform, the revised formulation containing no chloroform may be marketed after submission of the supplemental application but prior to the receipt of written notice of its approval by the Food and Drug Administration.

(d) Any sponsor of a ''Notice of Claimed Investigational Exemption for a New Animal Drug'' (INAD notice) for an animal drug product containing chloroform as an ingredient shall amend the INAD notice on or before October 3, 1977, to revise the